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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,151	04/16/2002	Takashi Shigematsu	13723-002001	8643

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EXAMINER
PADMANABHAN, KARTIC

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 10/05/2004

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,151	SHIGEMATSU ET AL.	
	Examiner	Art Unit	
	Kartic Padmanabhan	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Priority

1. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Specification

2. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Objections

3. Claims 2-9, 11-13, and 17-19 objected to because of the following informalities: the claims should all begin "The method" instead of "A method". Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 7, 11, 13, and 16-19 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step is the way in which malondialdehyde is used to incorporate aldehyde into lipoprotein.

7. Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step is the way in which denatured lipoprotein is used as a standard to determine lipoprotein in blood or how it is used as an experimental reagent for investigating the role or physiological activity of denatured lipoprotein.

8. Claim 13 is rejected as vague and indefinite for the recitation of "capable" because it has been held that the recitation that an element is "capable of" performing a function is not a positive limitation but only requires the ability to so perform. It does not constitute a limitation in any patentable sense. *In re Hutchison*, 69 USPQ 138.

9. Claim 16 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step is the way in which the denatured lipoprotein of claim 15 is used as a standard for determining denatured lipoprotein.

10. Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step is the way in which denatured lipoprotein is used as a standard in a method for immunological determination.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1, 3, 8, 10, 12, and 14-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yamada et al. (JP 09-297137) in view of Lang et al. (EP 0 617 289).

Yamada et al. teach measuring a denatured or modified lipoprotein by use of an antibody which is not bound to a lipoprotein not denatured or modified, but specifically bonded to the denatured or modified lipoprotein. In this invention, the denatured or modified lipoprotein can be made by oxidation, reduction, disruption, heating or modifying agent. A polyclonal antibody or monoclonal antibody is used for measurement via enzyme immunoassay, fluorescent immunoassay, radiation immunoassay or the like. According to this method, a denatured or modified lipoprotein can be precisely measured without erroneously measuring lipoprotein not

denatured or modified, LDL and plasminogen. However, the reference does not teach lyophilization for stability (abstract).

Lang et al. teach the lyophilization of plasma or serum containing lipoprotein as being a stable composition (abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use lyophilization of Lang et al. with the process of denaturing lipoproteins of Yamada et al. because lyophilization adds stability to the composition as taught by Lang et al., and Lang teaches that lyophilization adds stability to composition containing lipoproteins.

15. Claims 2, 6, 11, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yamada et al. (JP 09-297137) in view of Lang et al. (EP 0 617 289) as applied to claims 1-2, 8, 10, 12, and 14-21 above, and further in view of Kimura (JP 09-288106).

Yamada and Lang teach methods, as previously discussed. However, the references do not teach human lipoprotein, using denatured lipoprotein as a standard, or a specific antibody.

Kimura et al. teach a measuring method for human lipoprotein oxide, in which lipoprotein oxide such as LDL oxide or the like in circulating blood can be detected with high sensitivity and quantitatively by a comparatively simple procedure. In a measuring method for human lipoprotein oxide, lipoprotein oxide in blood plasma is measured by using an antibody which recognizes an antigen generated by the oxidation of a phospholipid. In the measuring method, a compound obtained by artificially oxidizing the phospholipids and/or a combination of the compound of blood plasma protein are used as standard substances for measurement so as to be detected. When an antibody which recognizes an antigen generated by the oxidation of phosphatidylcoline under the coexistence of a peptide or an antibody obtained by sensitizing a proper animal by a gruel-like hardened focus is used as the antibody, an especially good result is

obtained. In addition, an antibody which is generated by hybridoma cell line FOHIa/DLH3 (Consignment No. FERM P-14153) is especially preferred (abstract).

It would have been *prima facie* obvious to use human lipoprotein, use denatured lipoprotein as a standard, and the specific antibody of Kimura et al. with the method of Yamada and Lang because one could have used any lipoprotein with the method of Yamada and Lang with a reasonable expectation of success. In addition, Kimura teaches that antibody which is generated by hybridoma cell line FOHIa/DLH3 is especially suited for detection of lipoprotein, and that denatured lipoprotein can be used as a standard in a variety of assays.

16. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable Yamada et al. (JP 09-297137) in view of Lang et al. (EP 0 617 289) as applied to claims 1-2, 8, 10, 12, and 14-21 above, and further in view of Hallahan et al. (US Pat. 5,969,040).

Yamada and Lang teach methods and compositions, as previously discussed. However, the references do not teach the use of HSA.

Hallahan et al. teach the use of HSA to stabilize a biological molecule.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use HSA of Hallahan et al. with the method of Yamada and Lang because Hallahan et al. teach that HSA is a known stabilizing agent.

17. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable Yamada et al. (JP 09-297137) in view of Lang et al. (EP 0 617 289) as applied to claims 1-2, 8, 10, 12, and 14-21 above, and further in view of Kondo et al. (US Pat. 6,248,545).

Yamada and Lang teach methods and compositions, as previously discussed. However, the references do not teach the use of malondialdehyde.

Kondo et al. teach the assay of denatured lipoprotein, wherein MDA-modified lipoprotein is one type of denatured lipoprotein.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use malondialdehyde to denature lipoprotein with the method of Yamada and Lang because Kondo et al. teach that malondialdeyhde modification is a way to effect lipoprotein denaturation.

18. Claims 4-5 are rejected under 35 U.S.C. 103(a) as being unpatentable Yamada et al. (JP 09-297137) in view of Lang et al. (EP 0 617 289) as applied to claims 1-2, 8, 10, 12, and 14-21 above, and further in view of Aviram et al. (US Pat. 6,362,236).

Yamada and Lang teach methods and compositions, as previously discussed. However, the references do not teach the use metal ions for oxidation.

Aviram et al. teach the oxidation of lipoproteins using metal ions, such as copper.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use copper ions to denature lipoprotein with the method of Yamada and Lang because Aviram et al. teach that copper ions may be used for denaturation purposes.

Conclusion

Claims 1-21 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kartic Padmanabhan whose telephone number is 571-272-0825. The examiner can normally be reached on M-F (8:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kartic Padmanabhan
Patent Examiner
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09/20/07